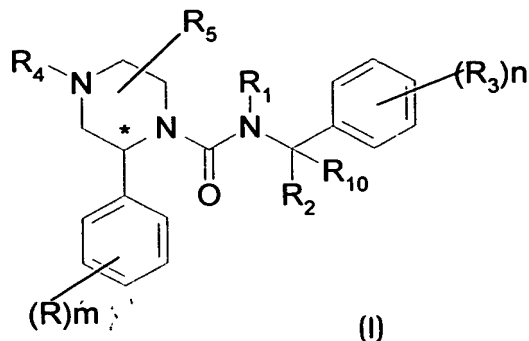


20. (Amended) A compound of formula (I)



wherein

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

R₂ is hydrogen, a C₁₋₄ alkyl, C₂₋₆ alkenyl or a C₃₋₇ cycloalkyl group; or R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively are a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy, or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂)_rCO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino, a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ are independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy, or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl group or

R₁₀ together with R₂ is a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3; n is zero or an integer from 1 to 3; both p and r are independently zero or an integer from 1 to 4; q is an integer from 1 to 4; provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively are a 5 to 6 membered heterocyclic group, i) m is 1 or 2; ii) when

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m is 1, R is not fluorine and iii) when m is 2, the two substituents R are not both fluorine,
or a pharmaceutically acceptable salt or solvate thereof.

21. (New) A compound as claimed in claim 1 wherein n is 2 and R₃ is trifluoromethyl both at the 3 and 5 position.

22. (New) A compound as claimed in claim 1 wherein R is selected independently from halogen or a C₁₋₄ alkyl group and m is 1 or 2.

23. (New) A compound as claimed in claim 1 wherein m is 2, R is selected independently from halogen or methyl group at 2 or 4 position.

24. (New) A compound as claimed in claim 1 wherein R₅ is hydrogen or a methyl group.

25. (New) A compound as claimed in claim 1 wherein R₁ is hydrogen or a methyl group.

26. (New) A compound as claimed in claim 1 wherein R₄ is hydrogen, a (CH₂)_rCO(CH₂)_pR₇ or CH₂)_qR₇ group, wherein R₇ represents an amine, both p and r are independently zero or 1; and q is 1 or 2.

27. (New) A compound of formula (I) as claimed in claim 1 wherein R is selected independently from halogen or methyl, R₃ is trifluoromethyl both at the 3 and 5 position, R₁ is hydrogen or methyl, R₂ is hydrogen, methyl, 2-propenyl or a cyclopropyl group or together with R₁ is a 3,6-dihydro-2H-pyridin-1-yl, a piperidin-1-yl or a pyrrolidin-1-yl group, R₁₀ represents hydrogen, a methyl or R₁₀ together with R₂ is a cyclopropyl group, R₄ is hydrogen, an aminoacetyl or amino ethyl group and R₅ is hydrogen or a methyl group.

28. (New) A compound of formula (I) as claimed in claim 1 wherein R is selected independently from halogen or methyl and m is 2, R₃ is trifluoromethyl both at the 3 and 5 position, R₁ and R₂ are independently hydrogen or methyl, R₄ is hydrogen and R₅ is hydrogen.

29. (New) A compound selected from:

- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-fluoro-phenyl)-piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-methyl-4-fluoro-phenyl)-6-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;

- 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- II* 2-(S)-(4-fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl)-methyl-amide];
- II* [2-(3,5-bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- II* [2-(3,5-bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(3,5-bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;
- and enantiomers, pharmaceutically acceptable salts, and solvates thereof.

30. (New) 2-(S)-(4-fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

31. (New) 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

B¹⁰ 32. (Amended) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methanesulphonate.

33. (New) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

34. (New) A pharmaceutical composition comprising a compound as claimed in claim 1 in admixture with one or more physiologically acceptable carriers or excipients.

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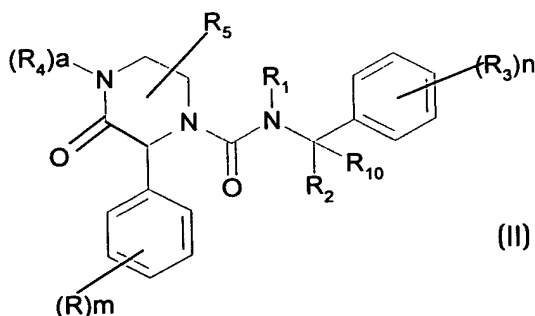
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35. (Amended) A method for the treatment of a condition mediated by a tachykinin, in a mammal, said method comprising administering an effective amount of a compound as claimed in claim 1.

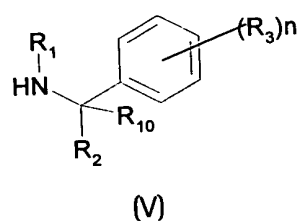
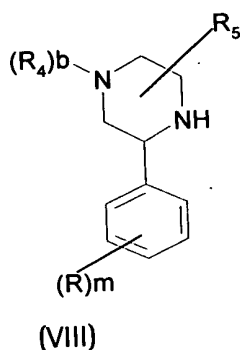
36. (Amended) The method of Claim 35 wherein said tachykinin is substance P or other neurokinins.

37. (New) The method of Claim 35 wherein said mammal is man.

38. (New) A process (A) for the preparation of a compound of formula (I) as claimed in claim 1, wherein R_4 is hydrogen or a $(CH_2)_qR_7$ group, provided that when R_5 is a C_{1-4} alkyl or a COR_6 group, R_5 is not in the 3 position of the piperazine ring, which comprises reduction of a compound of formula (II), wherein $(R_4)_a$ is hydrogen or a suitable nitrogen protecting group or $(R_4)_a$ is a $(CH_2)_qR_7$ group or protecting derivatives thereof; or



a process (B) for the preparation of a compound of formula (I) as claimed in claim 1, wherein R_4 is hydrogen or a $(CH_2)_r CO(CH_2)_p R_7$ group which comprises the reaction of a compound of formula (VIII), wherein $(R_4)_b$ represents a nitrogen protecting group or $(R_4)_b$ is $(CH_2)_r CO(CH_2)_p R_7$ or a protecting group thereof with triphosgene and an organic base followed by addition of the amine (V)

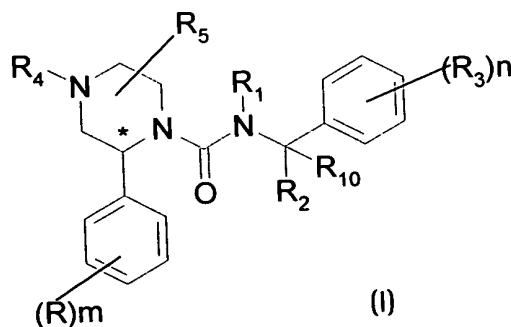


followed where necessary or desired by one or more of the following steps:

- (i) removal of any protecting group;
- (ii) isolation of the compound as salt thereof;
- (iii) separation of a compound of formula (I) or derivative thereof into the enantiomers thereof.

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39. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):



wherein:

R is a halogen atom or a C_{1-4} alkyl group;

contd.
B¹²

R₁ is hydrogen or a C₁₋₄ alkyl group;

R₂ is hydrogen, a C₁₋₄ alkyl, C₂₋₆ alkenyl or a C₃₋₇ cycloalkyl group; or R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂)_rCO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

i) m is 1 or 2;

ii) when m is 1, R is not fluorine and

iii) when m is 2, the two substituents R are not both fluorine,
or a pharmaceutically acceptable salt or solvate thereof.

40. (New) The method according to claim 39, wherein said mammal is man.

41. (New) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression, unipolar depression, single

*contd.
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major depressive episodes, recurrent major depressive episodes, dysthymic disorder, neurotic depression, social phobia, dementia of Alzheimer's type, vascular dementia with depressed mood, mood disorders induced by alcohol, mood disorders induced by amphetamines, mood disorders induced by cocaine, mood disorders induced by hallucinogens, mood disorders induced by inhalants, mood disorders induced by opioids, mood disorders induced by phencyclidine, mood disorders induced by sedatives, mood disorders induced by hypnotics, mood disorders induced by anxiolytics and schizoaffective disorder of the depressed type.

42. (New) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.

43. (New) The method according to claim 39, further comprising administering an effective amount of a serotonin reuptake inhibitor.

44. (New) The method according to claim 43, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.

45. (New) The method according to claim 39, further comprising administering an effective amount of a dopaminergic antidepressant.

46. (New) The method according to claim 45, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.

47. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

contd.
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- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- II 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;

*contd.
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[2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;
 or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.

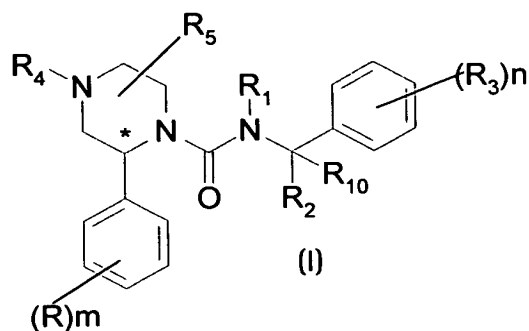
48. (New) The method according to claim 47, wherein said mammal is man.
49. (New) The method according to claim 47, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
50. (New) The method according to claim 47, further comprising administering an effective amount of a serotonin reuptake inhibitor.
51. (New) The method according to claim 50, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
52. (New) The method according to claim 47, further comprising administering an effective amount of a dopaminergic antidepressant.
53. (New) The method according to claim 52, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.

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54. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
55. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
56. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
57. (New) The method according to claim 56, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
58. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
59. (New) The method according to claim 58, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
60. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

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61. (New) The method according to claim 60, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.

62. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):



wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

R₂ is hydrogen, a C₁₋₄ alkyl, C₂₋₆ alkenyl or a C₃₋₇ cycloalkyl group; or R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂)_rCO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

contd.
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both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

i) m is 1 or 2;

ii) when m is 1, R is not fluorine and

iii) when m is 2, the two substituents R are not both fluorine,
or a pharmaceutically acceptable salt or solvate thereof.

63. (New) The method according to claim 62, wherein said mammal is a human.

64. (New) The method according to claim 62, further comprising administering an effective amount of a serotonin reuptake inhibitor.

65. (New) The method according to claim 64, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.

66. (New) The method according to claim 62, further comprising administering an effective amount of a dopaminergic antidepressant.

67. (New) The method according to claim 66, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.

68. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of

2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

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- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)-piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- II 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- II [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

contd.
B12 II

[2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;
or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.

69. (New) The method according to claim 68, wherein said mammal is a human.

70. (New) The method according to claim 68, further comprising administering an effective amount of a serotonin reuptake inhibitor.

71. (New) The method according to claim 70, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.

72. (New) The method according to claim 68, further comprising administering an effective amount of a dopaminergic antidepressant.

73. (New) The method according to claim 72, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.

74. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

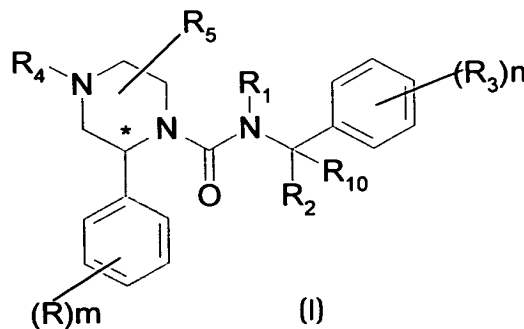
75. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

76. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.

77. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.

78. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

79. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):



wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

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R₁ is hydrogen or a C₁₋₄ alkyl group;

R₂ is hydrogen, a C₁₋₄ alkyl, C₂₋₆ alkenyl or a C₃₋₇ cycloalkyl group; or R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂)_rCO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

i) m is 1 or 2;

ii) when m is 1, R is not fluorine and

iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.

80. (New) The method according to claim 79, wherein said mammal is a human.

81. (New) The method according to claim 79, further comprising administering an effective amount of a serotonin reuptake inhibitor.

contd.
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82. (New) The method according to claim 81, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
83. (New) The method according to claim 79, further comprising administering an effective amount of a dopaminergic antidepressant.
84. (New) The method according to claim 83, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.
85. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;

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2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;

4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;

II 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;

II [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

II [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;

2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;

2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;

or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.

86. (New) The method according to claim 85, wherein said mammal is a human.

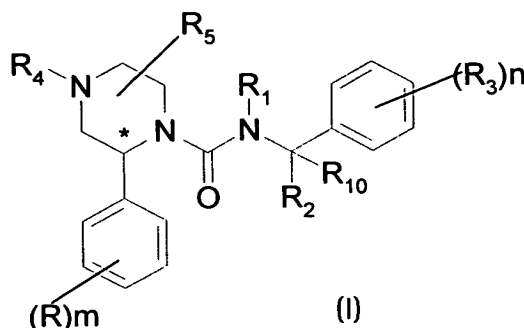
87. (New) The method according to claim 85, further comprising administering an effective amount of a serotonin reuptake inhibitor.

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88. (New) The method according to claim 87, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, citalopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
89. (New) The method according to claim 85, further comprising administering an effective amount of a dopaminergic antidepressant.
90. (New) The method according to claim 89, wherein said dopaminergic antidepressant is selected from the group consisting of bupropion and amineptine.
91. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
92. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
93. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
94. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.

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95. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

96. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):



wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

R₂ is hydrogen, a C₁₋₄ alkyl, C₂₋₆ alkenyl or a C₃₋₇ cycloalkyl group; or R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

R₃ is a trifluoromethyl, a C₁₋₄ alkyl, a C₁₋₄ alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)_qR₇ or a (CH₂)_rCO(CH₂)_pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms;

R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

contd.
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R₁₀ is hydrogen, a C1-4 alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;
 m is zero or an integer from 1 to 3;
 n is zero or an integer from 1 to 3;
 both p and r are independently zero or an integer from 1 to 4;
 q is an integer from 1 to 4;
 provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,
 i) m is 1 or 2;
 ii) when m is 1, R is not fluorine and
 iii) when m is 2, the two substituents R are not both fluorine,
 or a pharmaceutically acceptable salt or solvate thereof.

97. (New) The method according to claim 96, wherein said mammal is a human.
98. (New) The method according to claim 96, wherein said gastrointestinal disorder is irritable bowel syndrome.
99. (New) The method according to claim 96, further comprising administering an effective amount of a 5HT3 antagonist.
100. (New) The method according to claim 99, wherein said 5HT3 antagonist is selected from the group consisting of ondansetron, granisetron and metoclopramide.
101. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

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- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

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[2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;
 or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.

102. (New) The method according to claim 101, wherein said mammal is a human.

103. (New) The method according to claim 101, wherein said gastrointestinal disorder is irritable bowel syndrome.

104. (New) The method according to claim 101, further comprising administering an effective amount of a 5HT3 antagonist.

105. (New) The method according to claim 104, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.

106. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

107. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

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108. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.

109. (New) The method according to claim 108, wherein said gastrointestinal disorder is irritable bowel syndrome.

110. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.

111. (New) The method according to claim 110, wherein said gastrointestinal disorder is irritable bowel syndrome.

112. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

113. (New) The method according to claim 112, wherein said gastrointestinal disorder is irritable bowel syndrome.

114. (New) 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.